

Remarks

Claims 25-27, 29-35, 38-41, 43, 45-50, and 52-62 were pending in the subject application. By this Amendment, claims 25, 39, 40, 50, and 61 have been amended, and claims 29, 33, 34, 46-47, 53, and 59 have been cancelled. The undersigned avers that no new matter is introduced by this amendment. Accordingly, claims 25-27, 30-32, 35, 38, 39-41, 43, 45, 48-50, 52, 54-58, and 61-62 are currently before the Examiner for consideration. Favorable consideration of the pending claims is respectfully requested.

The applicants gratefully acknowledge the Examiner's withdrawal of the rejections under 35 U.S.C. §112, first and second paragraphs.

Claims 25-27, 35, 38-40, 43, 48, 49, and 59 have been rejected under 35 U.S.C. §102(b) as being anticipated by Hadley *et al.* (*J. Cell. Biol.*, 1985, 101:1511-1522). The applicants respectfully submit that the Hadley *et al.* publication does not teach or suggest the applicants' claimed invention. However, the applicants have amended the claims in order to lend greater clarity to the claimed subject matter and to expedite prosecution of the subject application.

Claims 25, 39, and 40 have been amended to recite the limitation of claim 29, *i.e.*, that the non-Sertoli cells are selected from the group consisting of neuronal cells, NT2 cells, pancreatic islet cells, dopaminergic cells, and bovine chromaffin cells. Claim 29 was not included in the rejection under 35 U.S.C. §102(b). The Hadley *et al.* publication does not teach co-culture of Sertoli cells with any of the recited non-Sertoli cells, or biochambers having a lumen containing the recited non-Sertoli cells. Claim 59 has been cancelled.

Additionally, the applicants note that claim 38 is included in the rejection under 35 U.S.C. §102(b). Claim 38 recites that the biochamber is spherical in shape. The Office Action does not indicate where the Hadley *et al.* publication describes spherical structures, and no such description is apparent to the applicants. For example, although Figure 5b of the Hadley *et al.* publication appears to depict a spherical structure, this is actually a cross-section of a cord, which is tubular in shape (see page 1517, second column, and Figure 3a).

It is well settled in patent law that, in order to anticipate under 35 U.S.C. §102, a single reference must disclose within the four corners of the document each and every element and

limitation contained in the rejected claims. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991). The applicants respectfully submit that the cited reference does not teach every element of the applicants' claimed invention and, therefore, does not anticipate the applicants' claimed invention. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

Claims 25, 29, 30, 33, 34, 40, 46, 47, 50, and 52-56 have been rejected under 35 U.S.C. §103(a) as being obvious over Selawry (U.S. Patent No. 5,843,430) in view of Hadley *et al.* Claims 25, 29-34, 40, 46, 47, 50, and 52-56 have also been rejected under 35 U.S.C. §103(a) as being obvious over Sanberg *et al.* (U.S. Patent No. 5,942,437) in view of Hadley *et al.* Claims 45, 57, 59, and 60 have also been rejected under 35 U.S.C. §103(a) as being obvious over Sanberg *et al.* and Hadley *et al.* and further in view of van der Wee *et al.* (*Exp Cell Res*, 1999, 252:175-185). In addition, claims 41, 58, 61, and 62 have been rejected under 35 U.S.C. §103(a) as being obvious over Sanberg *et al.*, Hadley *et al.* and van der Wee *et al.*, and further in view of Spaulding (U.S. Patent No. 6,001,643). The applicants respectfully submit that the cited references, alone or in combination, do not teach or suggest the applicants' claimed invention. However, as indicated above, the applicants have amended the claims in order to lend greater clarity to the claimed subject matter and to expedite prosecution of the subject application.

Claims 25, 39, and 40 have been amended to recite the limitation of claim 29, *i.e.*, that the non-Sertoli cells are selected from the group consisting of neuronal cells, NT2 cells, pancreatic islet cells, dopaminergic cells, and bovine chromaffin cells. Claim 50 has been amended to recite the limitation of claim 53, *i.e.*, that the non-Sertoli cells are therapeutic cells.

As indicated above in response to the rejection under 35 U.S.C. §102(b), the Hadley *et al.* reference does not teach the biochambers of the subject invention as currently claimed. The Hadley *et al.* reference does not teach biochambers having a lumen containing neuronal cells, NT2 cells, pancreatic islet cells, dopaminergic cells, or bovine chromaffin cells.

The Office Action indicates that the Hadley *et al.* publication teaches a method comprising "co-culturing Sertoli cells and non-Sertoli cells (germ cells)". However, the non-Sertoli cells described in the Hadley *et al.* publication are merely testicular cell contaminants from the Sertoli cell enzymatic isolation procedure. As described in the "Sertoli Cell Preparation" section at page 1512,

column 2, lines 24-27, of the Hadley *et al.* publication, "this procedure yields Sertoli cell aggregates of 10-50 cells that contain a 1-5% contamination of germ cells (only up to type B spermatogonia), a 1-2% contamination of myoid cells, and very small (<1%) contamination of Leydig and fibroblastic cells". Furthermore, although co-culture of Sertoli cells and myoid cells is described in the Hadley *et al.* publication, this was only carried out to produce a detergent-extracted Sertoli-myoid matrix, which served as a substrate for Sertoli cell growth (see page 1512, first column, lines 31-33, and second column, lines 30-41). The Hadley *et al.* publication is directed toward the study of the interaction between Sertoli cells and germ cell differentiation. As indicated at page 1522 of the Hadley *et al.* publication,

we have demonstrated for the first time that germ cell differentiation can progress (from spermatogonia to late pachytene spermatocytes) in primary cultures of dissociated Sertoli cells. This provides the first evidence that the blood-testis barrier is necessary for germ cell development. The degree of differentiation maintained by Sertoli cells grown on top of or within RBM indicates that these cultures will prove to be a valuable tool with which to dissect the complex interactions among Sertoli, myoid, and germ cells within the testis.

There is no suggestion of co-culturing Sertoli cells and therapeutic cells, such as neurons or islets, to produce the biochambers of the subject invention. There is nothing within any of the cited references that teaches or suggests that non-testicular cells, such as neurons or islets, could be substituted for the germ cell contaminants such that the Sertoli cells would compartmentalize, form Sertoli-Sertoli tight junctions, and incorporate the non-testicular cells into the luminal compartment, with any reasonable expectation of success. Moreover, there is no suggestion to use such structures as transplantation units in cell therapy.

At pages 5 and 6, the Office Action indicates that "because the therapeutic cells surrounded by Sertoli cells having the tight junction would provide better protection for therapeutic cells, preventing or reducing a host immune response." Only the subject specification teaches that the tight junctions that develop between adjacent Sertoli cells when the Sertoli cells are cultured in the presence of a basement membrane preparation can be exploited to protect therapeutic cells that become incorporated into the lumen of the resulting biochamber. The Selawry and Sanberg patents only teach the benefits of co-culture and co-transplantation of Sertoli cells and therapeutic cells in

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general. The van der Wee and Spaulding references do not cure the deficiencies of the other references.

As a matter of law, a finding of obviousness is proper only when the prior art contains a suggestion or teaching of the claimed invention. Here, it is only the applicants' disclosure that provides such a teaching, and the applicants' disclosure cannot be used to reconstruct the prior art for a rejection under §103. This was specifically recognized by the CCPA in *In re Spinnoble*, 56 CCPA 823, 160 USPQ 237, 243 (1969):

The Court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is we must review the prior art without reading into that art appellant's teachings. *In re Murray*, 46 CCPA 905, 268 F.2d 226, 112 USPQ 364 (1959); *In re Sprock*, 49 CCPA 1039, 301 F.2d 686, 133 USPQ 360 (1962). The issue, then, is whether the teachings of the prior art would, in and of themselves and without the benefits of appellant's disclosure, make the invention as a whole, obvious. *In re Leonor*, 55 CCPA 1198, 395 F.2d 801, 158 USPQ 20 (1968). (Emphasis in original)

There mere fact that the purported prior art could have been modified or applied in a manner to yield applicants' invention would not have made the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Moreover, as expressed by the CAFC, to support a §103 rejection, "[b]oth the suggestion and the expectation of success must be founded in the prior art. . . ." *In re Dow Chemical Co.*, 5 USPQ 2d 1529, 1531, (Fed. Cir. 1988). In the references cited in support of the §103 rejections, one finds neither. The cited references do not teach or suggest the claimed biochambers or methods of transplantation using such biochambers. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejections under §103(a).

In view of the foregoing remarks and amendments to the claims, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

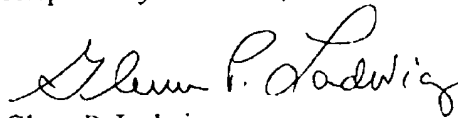
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The applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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